231. (New) The method of Claim 192 wherein said antibody or antigen-binding fragment is selected from the group consisting of a human antibody, a humanized antibody, a chimeric antibody and an antigen-binding fragment of any one of the foregoing.

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232. (New) The method of Claim 192 wherein said antibody or antigen-binding fragment is an antigen-binding fragment selected from the group consisting of a Fab fragment, a Fab' fragment, a $F(ab')_2$ fragment and a Fv fragment.

REMARKS

Claims 46-50, 76-145, 147 and 202-216 have been cancelled without prejudice. Claims 146, 148, 149, 151, 153, 154, 157, 160-164, 170-174, 180-182, 190-192, 200 and 201 have been amended, and new Claims 217-232 have been added to the application. Claims 146, 148-201 and 217-232 are pending.

Claims 146, 162 and 172 have been amended to recite that the antibody or antigen-binding fragment thereof binds mammalian GPR-9-6 and inhibits binding of TECK to said mammalian GPR-9-6. Support for the amendments is found at page 18, line 26 *et seq.*

Claims 162 and 172 have been further amended to recite that the mammalian GPR-9-6 is recognized by mAb 3C3 or mAb GPR96-1, respectively. Support for the amendments is found at page 19, line 16 through page 20, line 27.

Claims 182 and 192 have been amended to recite that the antibody or antigen-binding fragment thereof has the epitopic specificity of mAb 3C3 or mAb GPR96-1, respectfully. Support for the amendments is found at page 19, line 16 through page 20, line 27.

The amended claims more clearly set forth the characteristics of the mammalian GPR-9-6 and of the antibody or antigen-binding fragment used in the claimed methods. The method of Claims 146, 148-181 and 217-228 does not require that the binding of TECK to a mammalian GPR-9-6 be inhibited in performing the method, although the antibody or antigen-binding fragment used has the property of inhibiting binding of TECK to a mammalian GPR-9-6.

Further remarks are set forth below with reference to the numbered paragraphs of the Office Action.

Paragraph 4. Species Election

The undersigned affirms the election of an agent which inhibits a function of GPR-9-6 as the species of agent which modulates a function of GPR-9-6.

Paragraph 8. Drawings

A Transmittal of Formal Drawings and Formal Drawings are being filed concurrently herewith. Acceptance of the Formal Drawings is requested.

Paragraph 9. Related Application Paragraph

The Related Application Paragraph has been updated to indicate that U.S. Application No. 09/266,464 has now issued as U.S. Patent No. 6,329,159 B1.

Paragraph 11. Objection to the Title

The title has been amended to more clearly indicate the subject matter of the claims.

Paragraph 14. Rejection of Claims 46-50, 78-85, 89, 90, 93-95, 99-109, 111-114, 117-146 and 148-201 Under 35 U.S.C. § 112, First Paragraph

Claims 46-50, 78-85, 89, 90, 93-95, 99-109, 111-114, 117-146 and 148-201 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The rejection is based on the recitation of "GPR-9-6," "mammalian GPR-9-6," "agent which binds" GPR-9-6, and/or "ligand" of GPR-9-6 in the claims.

The Examiner states that the specification discloses human GPR-9-6 of SEQ ID NO:2 which is bound by mAb 3C3 and mAb GPR96-1, but does not provide adequate support for the genus of GPR-9-6 or the genus of mammalian GPR-9-6. (Office Action at page 5, lines 20-25.) The Examiner further states that the specification discloses that TECK is a chemokine ligand of GPR-9-6, but that the disclosure of TECK and of antibodies that bind GPR-9-6 does not provide adequate support for the genus of ligands or the genus of agents which bind GPR-9-6. (Office Action at page 5, lines 26-31.)

Claims 46-50, 78-85, 89, 90, 93-95, 99-109, 111-114 and 117-145 have been cancelled without prejudice, thereby obviating the rejection with respect to these claims.

Independent Claims 146, 162 and 172 have been amended to recite that the antibody or antigen-binding fragment thereof used in the method is one which inhibits binding of TECK to the mammalian GPR-9-6. Independent Claim 162 has been further amended to recite that the mammalian GPR-9-6 is recognized by mAb 3C3 and binds TECK, and independent Claim 172 has been further amended to recite that the mammalian GPR-9-6 is recognized by mAb GPR96-1 and binds TECK. Independent Claims 182 and 192 have been amended to recite that the antibody or antigen-binding fragment thereof has the epitopic specificity of mAb 3C3 or mAb GPR96-1, respectively.

The claims, as amended, recite structural features or immunochemical properties, and ligand binding properties shared by members of the recited mammalian GPR-9-6 genus. These recited features and properties are sufficient to distinguish the mammalian GPR-9-6 from other materials, and the genus does not have substantial variation because the member of the genus have at least about 90% amino acid sequence similarity to SEQ ID NO:2 and bind TECK, or are recognized by mAb 3C3 or mAb GPR96-1 and bind TECK. Accordingly, the disclosure of a GPR-9-6 having the amino acid sequence of SEQ ID NO:2, and the exemplification of two antibodies (mAb 3C3 and mAb GPR96-1) that bind GPR-9-6 and inhibit binding of TECK to the receptor, is sufficient to convey to the person of skill in the art that Applicants were in possession of the claimed methods. Reconsideration and withdrawal of the rejection are requested.

Paragraph 15. Rejection of Claims 46-50, 78-85, 89, 90, 93-95, 99-109, 111-114, 117-146 and 148-201 Under 35 U.S.C. § 112, First Paragraph

Claims 46-50, 78-85, 89, 90, 93-95, 99-109, 111-114, 117-146 and 148-201 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to make and use the invention commensurate in scope with the claims. The Examiner states that the specification does not reasonably provide enablement for any "GPR-9-6," any "mammalian GPR-9-6," any "agent," or any "ligand." However, the Examiner acknowledges that the specification is enabling for

A) a GPR-9-6 recognized by mAb 3C3 or mAb GPR96-1, the GPR-9-6 of SEQ ID NO:2, and a GPR-9-6 that binds TECK and is at least about 90% similar to the amino acid sequence of SEQ ID NO:2;

B) an agent that is a antibody that binds GPR-9-6 and an agent that is the chemokine TECK;

C) a ligand that is TECK. (Office Action at page 6, lines 3-11.)

Claims 46-50, 78-85, 89, 90, 93-95, 99-109, 111-114 and 117-145 have been cancelled without prejudice, thereby obviating the rejection with respect to these claims.

Independent Claims 146, 162 and 172 have been amended to recite that the antibody or antigen-binding fragment thereof inhibits binding of TECK to the mammalian GPR-9-6. Independent Claim 162 has been further amended to recite that the mammalian GPR-9-6 is recognized by mAb 3C3 and binds TECK, and independent Claim 172 has been further amended to recite that the mammalian GPR-9-6 is recognized by mAb GPR96-1 and binds TECK. Independent Claims 182 and 192 have been amended to recite that the antibody or antigen-binding fragment thereof has the epitopic specificity of mAb 3C3 or mAb GPR96-1, respectively. Accordingly, independent Claims 146, 162, 172, 182 and 192 are drawn to subject matter that the Examiner acknowledges to be enabled. Withdrawal of the rejection with respect to independent Claims 146, 162, 172, 182 and 192 and claims dependent from these claims is requested.

Paragraph 16. Rejection of Claims 103, 121, 141, 157, 167, 177, 187 and 197 Under 35 U.S.C. § 112, First Paragraph

Claims 103, 121, 141, 157, 167, 177, 187 and 197 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. The Examiner states that it is unclear whether the MOLT-13 cell line is readily available to the public, and invites Applicants to provide evidence that this cell line is readily available.

Provided herewith is a page from the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) on line catalog showing that the MOLT-13 cell line is available

from this depositary. (Reference AX3 in the Third Supplemental Information Disclosure Statement filed concurrently herewith.) DSMZ is a recognized International Depositary Authority under the Budapest Treaty. Withdrawal of the rejection is requested.

Paragraph 21. Rejection of Claims 46-48, 79-85, 89, 90, 94, 99-109 and 117-129 Under 35 U.S.C. § 112, Second Paragraph

Claims 46-48, 79-85, 89, 90, 94, 99-109 and 117-129 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 46-48, 79-85, 89, 90, 94, 99-109 and 117-129 have been cancelled without prejudice, thereby obviating the rejection.

Paragraph 23. Rejection of Claims 46, 89, 90, 93-95, 99, 100, 102, 104-109, 117, 118, 120, 122, 123 and 126-129 Under 35 U.S.C. § 102(b)

Claims 46, 89, 90, 93-95, 99, 100, 102, 104-109, 117, 118, 120, 122, 123 and 126-129 are rejected under 35 U.S.C. § 102(b) as being anticipated by Vicari *et al.* (*Immunity, 7*:291-301 (1997); Reference AV or record) as evidenced by Zabel *et al.* (*J. Exp. Med., 190*:1241-1255 (1999); Reference AR3 of record).

Claims 46, 89, 90, 93-95, 99, 100, 102, 104-109, 117, 118, 120, 122, 123 and 126-129 have been cancelled without prejudice, thereby obviating the rejection.

Information Disclosure Statement

A Supplemental Information Disclosure Statement (SIDS) is being filed concurrently herewith. Acknowledgment of consideration of the information provided therein is respectfully requested in the next Office Communication.

Applicants have received initialed copies of the Form 1449 provided with the Information Disclosure Statement filed on August 14, 2000 that indicate which references have been considered. All references cited on the Form 1449 were initialed by the Examiner except Reference AA (Murphy *et al.*, U.S. Patent No. 5,652,1333). The Examiner is requested to

consider Reference AA if she has not already, and to acknowledge that the reference has been considered in the next Office Communication.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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Concord, MA 01742-9133
Dated: March 31, 2003

MARKED UP VERSION OF AMENDMENTS

Specification Amendments Under 37 C.F.R. § 1.121(b)(1)(iii)

Replace the title on page 1, with the below title marked up by way of bracketing and strike out, and underlining to show the changes relative to the previous version of the paragraph.

[~~ANTI-GPR-9-6 ANTIBODIES AND~~] METHODS OF [~~IDENTIFYING MODULATORS OF~~] INHIBITING GPR-9-6 FUNCTION

Replace the Related Application paragraph on page 1, with the below paragraph marked up by way of bracketing and strike out, and underlining to show the changes relative to the previous version of the paragraph.

This application is a continuation-in-part of U.S.S.N. 09/266,464, filed March 11, 1999, now U.S. Patent No. 6,329,159 B1, the entire teachings of which are incorporated herein by reference.

Replace the title on page 92, with the below title marked up by way of bracketing and strike out, and underlining to show the changes relative to the previous version of the paragraph.

[~~ANTI-GPR-9-6 ANTIBODIES AND~~] METHODS OF [~~IDENTIFYING MODULATORS OF~~] INHIBITING GPR-9-6 FUNCTION

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

Claims 46-50, 76-145, 147 and 202-216 have been cancelled. New Claims 217-232 have been added to the application.

146. (Amended) A method of inhibiting a function of GPR-9-6 comprising contacting a cell that expresses a mammalian GPR-9-6 with an antibody or antigen-binding fragment thereof which binds said mammalian GPR-9-6 and inhibits binding of [~~a ligand~~] TECK to said

mammalian GPR-9-6, wherein said mammalian GPR-9-6 binds TECK and comprises an amino acid sequence that is at least about 90% similar to the amino acid sequence of SEQ ID NO:2.

148. (Amended) The method of Claim 146 wherein the binding of said antibody or said antigen-binding fragment to said mammalian GPR-9-6 [~~can be~~] is inhibited by a peptide that consists of the amino acid sequence of SEQ ID NO:3.

149. (Amended) The method of Claim 146 wherein the binding of said antibody or antigen-binding fragment to said mammalian GPR-9-6 [~~can be~~] is inhibited by mAb 3C3 (ATCC Accession No. HB-12653).

151. (Amended) The method of Claim 146 wherein the binding of said antibody or antigen-binding fragment to said mammalian GPR-9-6 [~~can be~~] is inhibited by mAb GPR96-1 (ATCC Accession No. PTA-1470).

153. (Amended) The method of Claim 146 wherein said mammalian GPR-9-6 is a human GPR-9-6.

154. (Amended) The method of Claim 146 wherein said mammalian GPR-9-6 comprises the amino acid sequence of SEQ ID NO:2.

157. (Amended) The method of Claim 156 wherein said cell line is selected from the group consisting of MOLT-4 and MOLT-13.

160. (Amended) The method of Claim 146 wherein said cell that expresses a mammalian GPR-9-6 is contacted with said [~~agent~~] antibody or antigen-binding fragment thereof *in vitro*.

161. (Amended) The method of Claim 146 wherein said cell that expresses a mammalian GPR-9-6 is contacted with said [~~agent~~] antibody or antigen-binding fragment thereof *in vivo*.

162. (Amended) A method of inhibiting a function of GPR-9-6 comprising contacting a cell that expresses a mammalian GPR-9-6 with an antibody or antigen-binding fragment thereof which binds said mammalian GPR-9-6 and inhibits binding of [~~a ligand~~] TECK to said mammalian GPR-9-6, wherein said [~~antibody or said antigen-binding fragment has the epitopic specificity of~~] mammalian GPR-9-6 is recognized by mAb 3C3 (ATCC Accession No. HB-12653) and binds TECK.

163. (Amended) The method of Claim 162 wherein said mammalian GPR-9-6 is a human GPR-9-6.

164. (Amended) The method of Claim 162 wherein said mammalian GPR-9-6 comprises the amino acid sequence of SEQ ID NO:2.

170. (Amended) The method of Claim 162 wherein said cell that expresses a mammalian GPR-9-6 is contacted with said antibody or antigen-binding fragment *in vitro*.

171. (Amended) The method of Claim 162 wherein said cell that expresses a mammalian GPR-9-6 is contacted with said antibody or antigen-binding fragment *in vivo*.

172. (Amended) A method of inhibiting a function of GPR-9-6 comprising contacting a cell that expresses a mammalian GPR-9-6 with an antibody or antigen-binding fragment thereof which binds said mammalian GPR-9-6 and inhibits binding of [~~a ligand~~] TECK to said mammalian GPR-9-6, wherein said [~~antibody or said antigen-binding fragment has the epitopic specificity of~~] mammalian GPR-9-6 is recognized by mAb GPR96-1 (ATCC Accession No. PTA-1470) and binds TECK.

173. (Amended) The method of Claim 172 wherein said mammalian GPR-9-6 is a human GPR-9-6.

174. (Amended) The method of Claim 172 wherein said mammalian GPR-9-6 comprises the amino acid sequence of SEQ ID NO:2.

180. (Amended) The method of Claim 172 wherein said cell that expresses a mammalian GPR-9-6 is contacted with said antibody or antigen-binding fragment *in vitro*.

181. (Amended) The method of Claim 172 wherein said cell that expresses a mammalian GPR-9-6 is contacted with said antibody or antigen-binding fragment *in vivo*.

182. (Amended) A method of inhibiting a function of GPR-9-6 comprising contacting a cell that expresses a GPR-9-6 with an antibody or antigen-binding fragment thereof that [~~binds said GPR-9-6 and inhibits the binding of a ligand to said GPR-9-6~~] has the epitopic specificity of mAb 3C3 (ATCC Accession No. HB-12653), wherein said GPR-9-6 binds TECK and comprises an amino acid sequence that is at least about 90% similar to the amino acid sequence of SEQ ID NO:2[~~; and said antibody or said antigen-binding fragment has the epitopic specificity of mAb 3C3 (ATCC Accession No. HB-12653)~~].

190. (Amended) The method of Claim 182 wherein said cell that expresses a mammalian GPR-9-6 is contacted with said antibody or antigen-binding fragment *in vitro*.

191. (Amended) The method of Claim 182 wherein said cell that expresses a mammalian GPR-9-6 is contacted with said antibody or antigen-binding fragment *in vivo*.

192. (Amended) A method of inhibiting a function of GPR-9-6 comprising contacting a cell that expresses a GPR-9-6 with an antibody or antigen-binding fragment thereof that [~~binds said GPR-9-6 and inhibits the binding of a ligand to said GPR-9-6~~] has the epitopic specificity of mAb GPR96-1 (ATCC Accession No. PTA-1470), wherein said GPR-9-6 binds TECK and comprises an amino acid sequence that is at least about 90% similar to the amino acid

sequence of SEQ ID NO:2[~~; and said antibody or said antigen-binding fragment has the epitopic specificity of mAb GPR96-1 (ATCC Accession No. PTA-1470)~~].

200. (Amended) The method of Claim 192 wherein said cell that expresses a mammalian GPR-9-6 is contacted with said antibody or antigen-binding fragment *in vitro*.

201. (Amended) The method of Claim 192 wherein said cell that expresses a mammalian GPR-9-6 is contacted with said antibody or antigen-binding fragment *in vivo*.